

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-8. (cancelled)

9. (previously presented) A polypeptide analog of *Bordetella pertussis* toxin S1 subunit, said analog differing in the amino acid sequence from that of naturally occurring S1 subunit by substitution of a different amino acid residue at arginine 9, wherein the analog has a biological activity which (a) can elicit toxin-neutralizing levels of antibodies and (b) is substantially free of enzymatic activities associated with toxin reactogenicity.

10. (cancelled)

11. (original) The analog of claim 9 wherein said toxin-neutralizing levels of antibodies provide immunoprotection against *Bordetella* toxicity.

12. (previously presented) The analog of claim 9 wherein said biological activity of (b) is obtained by site-specific mutagenesis resulting in said analog being substantially inactive enzymatically.

13-14. (cancelled)

15. (previously presented) The analog of claim 9 wherein said arginine 9 is replaced with lysine.
16. (cancelled)
17. (previously presented) The analog of claim 9 which includes an amino-terminus methionylvalyl sequence.
18. (previously presented) An analog of *Bordetella pertussis* toxin S1 subunit, said analog comprising an amino acid sequence as depicted in Figure 7 (SEQ ID NO: 27), said analog having a biological activity which (a) can elicit toxin-neutralizing levels of antibodies and (b) is substantially free of enzymatic activities associated with toxin reactogenicity.
19. (previously presented) A vaccine against pertussis comprising a modified *Bordetella pertussis* toxin in which a different amino acid residue has been substituted for arginine 9 in subunit S1, wherein the modified *Bordetella pertussis* toxin has a biological activity which (a) can elicit toxin-neutralizing levels of antibodies and (b) is substantially free of enzymatic activities associated with toxin reactogenicity.
20. (cancelled)
21. (previously presented) The vaccine of claim 19 wherein said toxin-neutralizing levels of antibodies provide immunoprotection against *Bordetella* toxicity.

22-24. (cancelled)

25. (previously presented) The vaccine of claim 19 wherein arginine 9 is replaced with lysine.

26-34. (cancelled)

35. (previously presented) A vaccine against pertussis comprising a polypeptide analog of *Bordetella pertussis* toxin subunit S1 comprising an amino acid sequence depicted in Figure 7 (SEQ ID NO: 27), said analog having a biological activity which (a) can elicit toxin-neutralizing levels of antibodies and (b) is substantially free of enzymatic activities associated with toxin reactogenicity.

36. (new) An immunoprotective *Bordetella pertussis* toxin S1 subunit analog wherein at least arginine at the ninth position from the mature N-terminus in the S1 subunit has been substituted with a different amino acid to reduce the toxicity without adversely affecting the immunological properties, and wherein the toxin S1 subunit analog is produced by the process of a) site-directed mutagenesis of the native pertussis toxin S1 subunit gene and b) expression of said gene mutated by site-directed mutagenesis.

37. (new) The *Bordetella pertussis* toxin S1 subunit analog of claim 36 in which lysine has been substituted for said arginine.

38. (new) A vaccine against *Bordetella pertussis*, comprising an effective amount of an immunoprotective, genetically-detoxified *Bordetella pertussis* toxin comprising an S1 subunit

analog wherein at least arginine at the ninth position from the mature N-terminus in the S1 subunit has been substituted with a different amino acid, thereby reducing the ADP-ribosyltransferase activity of the S1 subunit, and wherein said vaccine is produced by the process of a) site-directed mutagenesis of the native pertussis toxin S1 subunit gene, b) expression of said gene mutated by site-directed mutagenesis, and c) incorporation of the S1 subunit analog into a toxin molecule.

39. (new) The vaccine of claim 38 in which lysine has been substituted for said arginine.

40. (new) A vaccine comprising a *Bordetella pertussis* toxin S1 subunit analog in which at least the arginine residue at the ninth position from the mature N-terminus in the S1 subunit sequence has been substituted with another amino acid, wherein the S1 subunit analog, when expressed, is recognized by an antibody that confers immunoprotection against *Bordetella pertussis* and lacks enzymatic activity associated with *Bordetella pertussis* toxin reactogenicity, wherein the S1 subunit is produced by the process of a) site-directed mutagenesis of the native *Bordetella pertussis* toxin S1 subunit gene, and b) incorporation of said gene mutated by site-directed mutagenesis into a bacterial cell.

41. (new) The vaccine of claim 40 in which lysine has been substituted for said arginine.

42. (new) A polypeptide analog of the S1 subunit of *Bordetella pertussis*, said analog differing in amino acid sequence from that of the native S1 subunit sequence by at least one amino acid substitution including the substitution of a different amino acid residue at the arginine-9 position.

43. (new) The polypeptide analog of claim 42 wherein arginine is replaced with lysine at the arginine-9 position.